

**REMARKS/ARGUMENTS**

Applicants note that restriction between Groups IX and XII has been withdrawn, and have amended the elected claims accordingly. Applicants reserve the right to continue to prosecute claims included in groups that have not been elected, and claims included in nonelected portions of the elected claims, for example, to the use of compounds having formulas (Ib) and (Ic).

Applicants further note that the election of species was made provisionally, with the position that Applicants are entitled to generic claims if claims to the provisionally elected species are found allowable.

In the above amendment, elected method claims 90-95 had incorporated limitations of certain composition claims, which have not been elected. In making the amendment, claims 91, 92, 94 and 95 have been amended to specifically incorporate the composition limitations of claims on which they were dependent. However, these claims include material that has been restricted out, notably compounds in which X is group (Ib) or (Ic). Consequently, the marked-up claims show the deletion from their coverage of such compounds, typically by both underlining [to show the effective addition] and strikethrough [to show simultaneous, as it were, deletion]. In addition, as discussed below, the claims have been limited to focus on a group of AGP compounds which have been found to demonstrate unexpected properties when used in combinations with saponins.

Thus, claim 91 is marked up to show the exclusion of compounds in which X is group (Ib) or (Ic), together with elimination of definitions of substituents present only in such compounds. In addition, claim 91 has been amended to now define groups R<sub>1</sub>-R<sub>3</sub> as having from 10 to 14 carbon atoms, and to specify meanings for groups Y, Z, R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub> and R<sub>9</sub>, and subscripts m, n, p and q.

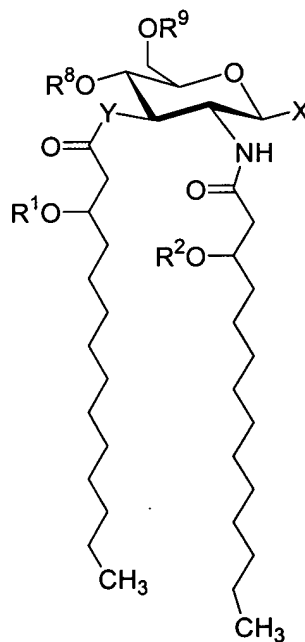
Claim 91 as thus amended, essentially reads:

91. A method of enhancing the immune response in an animal which comprises administering to the animal a composition comprising:

(a) at least one aminoalkyl glucosaminide phosphate (AGP); and

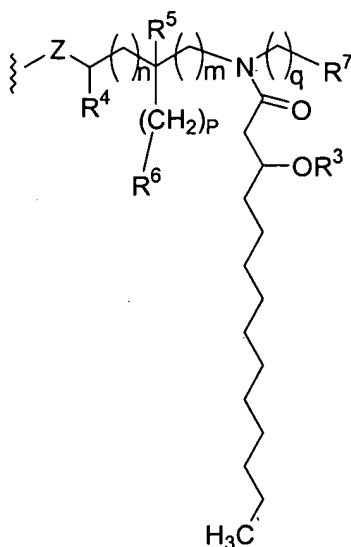
(b) at least one saponin;

wherein the AGP comprises a compound having the structure:



(I)

and pharmaceutically acceptable salts and derivatives thereof, wherein Y is -O-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from saturated and unsaturated (C<sub>10</sub>-C<sub>14</sub>)aliphatic acyl groups; R<sup>8</sup> is P(O)(OH)<sub>2</sub>; R<sup>9</sup> is -H; and X is



(Ia)

wherein the subscripts m and q are 0 and n and p are 0, 1, or 2; R<sup>3</sup> is a saturated or unsaturated optionally substituted aliphatic (C<sub>10</sub>-C<sub>14</sub>) acyl group; R<sup>4</sup> and R<sup>5</sup> are independently selected from H and methyl; R<sup>6</sup> is selected from H, OH and COOH, provided that the stereochemistry of the carbon atom to which R<sup>5</sup> is attached is not R when R<sup>6</sup> is OH or COOH; R<sup>7</sup> is H; and Z is -O-.

The definition of the AGP compounds in claim 94 is identical to that in claim 91.

Claims 90-95 are rejected as obvious over the combination of Johnson et al. and Kensil et al., further in view of "applicants' own admission". The "admission" referred to is Applicants' acknowledgment that the provisionally elected antigen, rDPV (rMtb8), is a known antigen.

The combination of Kensil et al. and Johnson et al., however, does not teach or suggest Applicants' claimed invention. Kensil et al. teach saponins useful as immune adjuvants, which include Quil A. Johnson et al. teach aminoalkyl glucosamine phosphate (AGP) compounds which are useful as adjuvants, including RC-529 (Compound B19 of this Application), variously formulated. However, the combination of Kensil and Johnson does not teach or suggest the combination of Quil A and RC-529, nor any other combination of saponins

and AGPs, nor does it teach or suggest that such a combination would be synergistic, as shown by the data in this Application.

One of skill in the art would appreciate that the mere combination of two or more adjuvants does not automatically result in a synergistic increase in activity of that combination compared to the individual components alone. The combined teachings of Kensil et al. and Johnson et al. do not teach the Applicants' unexpected findings of synergistic combinations of the claimed AGPs and saponins.

The claims of this Application are now limited to methods of use involving a small group of AGP compounds and, in preferred embodiments, Quillaja saponins, isotucarecol and an isotucarecol derivative. The data in the examples of this Application demonstrate synergistic activity of such compounds,

Example 1 (Tables 1 and 2) shows the unexpected improved results of combinations of AGP compounds B3 and B19 with the saponin Quil-A as compared with that saponin alone. Note particularly the unexpected activity of such combinations shown by the percent specific lysis in Table 2.

Example 2 (Table 3) shows unexpected and improved results obtained with a combination of AGP compound B19 and the saponin mimetic isotucarecol. Note particularly the vast improvement obtained when a small amount (5 µg) of B19 is added to compositions containing 1000 µg isotucarecol.

Example 3 (Table 4) shows unexpected and improved results obtained with combinations of AGP compound B19 and isotucarecol derivatives, particularly O-carboxymethylisotucarecol (B6).

Examples 4-8 show unexpected and improved results obtained with AGP compounds B3 and B19 in combination with the semisynthetic triterpenoid saponin GPI-0100.

### CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Appl. No. 10/068,171

PATENT

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If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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Attachments

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